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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/697,028	10/25/2000	Jeffrey Olson	11926-112001	3430

26161 7590 09/22/2003

FISH & RICHARDSON PC  
225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER
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CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 09/22/2003

*25*

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/697,028

Applicant(s)

STANTON, VINCENT P.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 10-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) (Paper NO. 23) filed on July 25, 2003. The request for RCE is accepted and is established with the status of the application as follows:

- a. the filling date of this RCE is established as 10/25/2000;
- b. Claims 10-16 are pending.

2. Applicants' response to the earlier office action (Paper No. 24) filed on July 25, 2003 is has been entered.

**Response to Arguments**

3. Applicant's response to the office action (Paper No.8) is fully considered. Applicants' arguments were addressed in the prior office action (advisory action, Paper No. 21) based on which Applicants filed the RCE.

4. With reference to the rejection maintained in the previous office action under 35 USC 102(e), the rejection is withdrawn in view of Applicants' amendment. Applicant's arguments with respect to claims 10-16 have been considered but are moot in view of the new ground(s) of rejection.

**New Grounds of rejections**

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Tyagi et.al. (USPN. 6,277,607) in view of Newton et al. (USPN. 5,595,890).

With regard to the instant claims 10 and 16, Tyagi et al. teach a method for biasing a DNA amplification reaction wherein a first nucleic acid molecule having a nucleotide at the polymorphic site is amplified to a greater extent than a second nucleic acid having a second, different nucleotide at the said polymorphic site (see column 12, lines 47-67 and column 13, lines 1-26). Tyagi et al. also disclose that the method comprises (i) contacting a sample of DNA with a pair of primers, one of which is complementary to a nucleic acid strand and the other of which is complementary to the other strand (see column 9, lines 12-25, column 11, lines 13-35), and amplifying the nucleic acid, thereby the polymorphic site with mutated nucleotide is amplified to a greater extend than the second or other nucleic acid molecule with a different nucleotide at the said site (column 8, lines 8-20, column 12, lines 47-67 and column 13, lines 1-26); Upon amplification the said primers form a stem-loop structure (hairpin stem) (see column 8, lines 39-66, column 9, lines 12-35);

With regard to the instant claims 11-15, Tyagi et al. also teach that the method comprises (i) DNA as a single-stranded or double-stranded DNA derived from human (see column 11, lines 5-67, column 12, lines 1-44); (ii) a series of polymerase chain reactions could be carried out to perform amplification of plurality of polymorphic sites (see column 12, lines 46-67, column 13, lines 1-25); determination of relative proportion of mutant and wild-type sequences in the amplified products (see column 8, lines 8-20).

Although Tyagi et al. teach mismatched primers substantially complementary to a target nucleic acid sequence, Tyagi et al. did not teach primers that do not hybridize to a polymorphic site.

Newton et al. teach a method for detecting one or more variant nucleotide sequences wherein Newton et al. teach that the method comprises primers having substantially complementary to target nucleic acid sequences (see column 11, lines 35-51), wherein Newton et al. disclose that to improve the specificity of priming of mismatches that do not result in hybridization to a target, and to avoid artefactual amplification products, one or more mismatched residues are deliberately added to the primers (see column 12, lines 15-26). Newton et al. also teach that the method could be adopted to detect haplotypes and more than one variant nucleotide in the same sample (see column 12, lines 27-46, column 13, lines 35-62).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of detecting a polymorphic site as taught by Tyagi et al. with a method for detecting one or more variants (alleles) which comprises a diagnostic primers having mismatches at a polymorphic site as taught by Newton et al. to achieve expected advantage of developing a sensitive and enhanced method for amplifying

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multiple alleles because Newton et al. suggests that “ an AA or CT mismatch does not normally result in hybridization, but a GT or AC mismatch may result in a sufficient degree of hybridization. Artefactual results may be avoided by deliberately introducing one or more further mismatched residues, or if desired, deletions or insertions, within diagnostic primer to destabilize the primer by further reducing binding during hybridization” (see column 12, lines 18-26). An ordinary practitioner would have been motivated to combine the teachings of Tyagi et al. with the teachings of Newton et al. because incorporating mismatched nucleotides with in primers corresponding to a polymorphic site as taught by Newton et al would improve the specificity of nucleic acid binding comprising specific variant nucleotides and reduce the nonspecific binding which reduces artefactual amplification products and aid in improving the detection of specific variant(s).

### ***Conclusion***

No claims are allowable.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chanduru  
September 16, 2003

  
**JEFFREY FREDMAN**  
**PRIMARY EXAMINER**